(19) World Intellectual Property Organization

International Bureau



. I TORRE BUILDING DE BERNE DER BERNE BERNE DER FOR DER BERNE BERNE BERNE BERNE BERNE BERNE BERNE BERNE BERNE

(43) International Publication Date 15 December 2005 (15.12.2005)

PCT

(10) International Publication Number WO 2005/118548 A1

- (51) International Patent Classification⁷: **C07D 217/18**, 401/06, A61K 31/472, 31/4725, A61P 3/04, 25/00
- (21) International Application Number:

PCT/EP2005/001879

- (22) International Filing Date: 23 February 2005 (23.02.2005)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

- PCT/EP2004/002020 1 March 2004 (01.03.2004) EP
- (71) Applicant (for all designated States except US): ACTE-LION PHARMACEUTICALS LTD [CH/CH]; Gewerbestrasse 16, CH-4123 Allschwil (CH).
- (72) Inventors; and
- (75) Inventors, and Inventors, applicants (for US only): WELLER, Thomas [CH/CH]; Hoelzlistrasse 58, CH-4102 Binningen (CH). KOBERSTEIN, Ralf [DE/DE]; Belchenstrasse 17, 79539 Lörrach (DE). AISSAOUI, Hamed [FR/FR]; 4, allée de Griottes, F-68840 Pulversheim (FR). CLOZEL, Martine [FR/CH]; Winterhalde 3b, CH-4102 Binningen (CH). FISCHLI, Walter [CH/CH]; Obertorweg 64, CH-4123 Allschwil (CH).

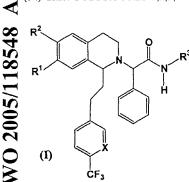
- (74) Agent: SCHAGER, Frank; Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED 1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES



(57) Abstract: The invention relates to novel 1,2,3,4-tetrahydroisoquinoline derivatives of formula (I) wherein R^1 , R^2 , R^3 and X are as defined in the claims, and their use as active ingredients in the preparation of pharmaceutical compositions. The invention also concerns related aspects including processes for the preparation of the compounds, pharmaceutical compositions containing one or more of those compounds and methods of treatment comprising administration of said compounds to a mammal.